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Brief Research Communication

Lujan-Fryns Syndrome in the Differential Diagnosis of Schizophrenia

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Schizophrenia is considered to be a heterogenous disorder. Different etiopathological mechanisms can be attributed to a similar clinical picture as described in DSM-III-R criteria. We present a case of a young man diagnosed on different occasions as schizophrenic with mild mental retardation. Clinical examination revealed signs and symptoms most compatible with the diagnosis of Lujan-Fryns syndrome, an X-linked mental retardation syndrome with marfanoid features, frequently associated with psychotic or other psychiatric symptoms. In all patients with symptoms of schizophrenia and mental retardation Lujan-Fryns syndrome should be considered in the differential diagnosis.

KEY WORDS: **schizophrenia, syndromology, psychiatric morbidity, X-linked retardation**

INTRODUCTION

In 1984, Lujan et al. reported a new X-linked mental retardation syndrome with mental retardation and marfanoid habitus as cardinal features. This specific form of X-linked mental retardation was further delineated by Fryns and Buttiens [1987], Laletta et al. [1991], Fryns [1991], Gurrieri and Neri [1991] and Spaepen et al. [1994]. Major phenotypic criteria are slight to moderate mental retardation, marfanoid habitus with excessive span, long slender hands and feet with short halluces and normal adult height, hypernasal voice, and distinct craniofacial anomalies. Patients also display behavior problems and frequently psychotic or other psychiatric symptoms.

We describe the history of a young man who had been diagnosed on different occasions as suffering from DSM-III-R [American Psychiatric Association, 1987] schizophrenia and mild mental retardation. Clinical examination revealed signs and symptoms compatible with Lujan-Fryns syndrome. In male patients presenting symptoms of both schizophrenia and mental retardation Lujan-Fryns syndrome should be considered in the differential diagnosis.

CLINICAL REPORT

R.S. is a 22-year-old male hospitalized in a psychiatric hospital for more than 4 years. Both parents, of Jewish origin, are healthy and nonrelated. Family history is negative with regard to mental handicap and psychiatric problems. He was born at the expected term as a floppy child and resuscitation was needed in the perinatal period. At the age of 1.5 years he started to walk but had poor psychomotor and coordination skills. Speech and language development were also delayed and initially congenital deafness was suspected. After the age of 7 years he attended special schools for children with psychomotor problems and learning disabilities.

At the age of 10 years the first behavioral problems appeared mainly consisting of impulsive, aggressive behavior. In a special institute for children with behavior problems and learning disabilities he received psychotropic medication (pimozide and oxazepam) for the first time at the age of 16. Clinical neurological examination was normal. Electrophysiological studies (electroencephalography and electromyography) did not reveal significant abnormalities. Extensive metabolic screening, including hexosaminidase-A, betagalactosidase, and arylsulfatases, was normal. Chromosome studies on peripheral blood lymphocyte culture revealed a 46, XY normal male karyotype after G-banding and fragile-X screening was negative.

At the age of 18 years he first reported hearing auditory hallucinations and persecutory delusions. The aggressive behavior remained unchanged. He was treated with haloperidol and zuclopenthixol. He was diagnosed as schizophrenic during hospitalization at a university hospital psychiatric ward and was transferred for further treatment to a psychiatric hospital.

The diagnosis was confirmed as schizophrenia, undifferentiated type, and mild mental retardation according to DSM-III-R-criteria [American Psychiatric Association, 1987]. Psychodiagnostic evaluation revealed a

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total IQ of 93 (Progressive Matrices) and performance IQ of 62. The positive psychotic symptoms did not respond to classical neuroleptics. Carbamazepine was added to control the impulsive and aggressive behavior.

The patient was referred to the Center of Human Genetics for further evaluation. Clinical examination revealed signs and symptoms most compatible with the diagnosis of Lujan-Fryns syndrome. He presented the characteristic phenotypical abnormalities with marfanoid habitus (height 182 cm, weight 62 kg, span 186.5 cm, head circumference 55.5 cm, right handlength 19.5 cm [19.4 cm = 97th percentile], right middle finger length 8 cm), mild midfacial, maxillary hypoplasia, generalized muscular hypotrophy with scapulae alatae, hyperkyphosis, pectus excavatum, and hypernasal voice (Fig. 1).

The psychotic disorder is fairly unresponsive to treatment. He is now taking a combination of risperidone and carbamezapine. He still suffers from auditory hallucinations, paranoid delusions, pronounced negative symptoms, and poor psychosocial functioning.

DISCUSSION

In the 1994 update not less than 127 different mental retardation syndromes with X-linked inheritance have been listed [Neri et al., 1994]. One of the most specific forms of X-linked mental retardation is the so-called X-linked mental retardation with marfanoid habitus as first reported by Lujan et al. [1984] and Fryns and Buttiens [1987]. Subsequently, Fryns [1991] delineated the clinical diagnostic criteria of this syndrome as follows: 1) Mild to moderate mental retardation. Lack of social integration due to emotional instability, shyness, and even psychotic behavior. 2) Marfanoid habitus with long, hyperextensible fingers and toes. However, halluces are short and second toes are relatively long. Adult height is normal. 3) Generalized hypotonia and hypernasal voice. 4) Normal secondary sexual development and normal testicular size. 5) Characteristic craniofacial appearance with large forehead, contrasting long and narrow face, maxillary hypoplasia, long nose with high and narrow nasal bridge, short and deep philtrum, thin upper lip, and highly arched palate.

From a psychiatric perspective the emotional and behavioral symptoms are interesting. In a review Spaepen et al. [1994] identified behavioral problems in 75% of the patients. In their own cohort of 14 boys with the typical phenotype a 100% rate of psychiatric disturbances was found. Two were extremely shy, 4 had been diagnosed as autistic, and 8 with the criteria for atypical pervasive developmental disorder. In their history one finds acute psychotic episodes. All patients were in some kind of psychiatric care (ambulatory or residential) and are in special education. Two of the 4 cases presented by Laletta et al. [1991] suffered from auditory hallucinations and showed passive, autistic behavior. Psychiatric disturbances are very common in this syndrome and may even be an essential part of it.

The history of the present patient confirms these findings. These psychiatric symptoms met the criteria for schizophrenia according to DSM-III-R [American Psychiatric Association, 1987]. The association between a schizophrenic syndrome and this X-linked mental retardation syndrome could be considered as possible further evidence for the hypothesis of an X chromosomal locus for schizophrenia [Crow, 1988; Delisi and Crow, 1989].

When a patient presents with symptoms of schizophrenia and mental retardation Lujan-Fryns syndrome should be considered in the differential diagnosis.

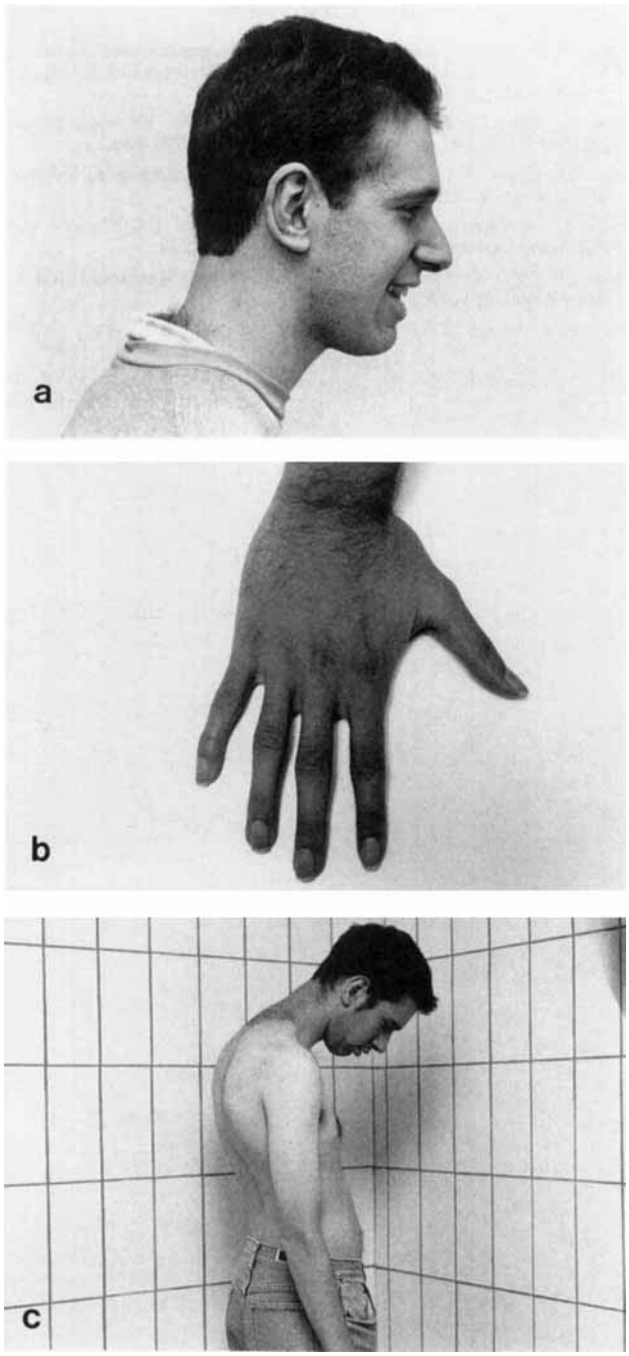

Fig. 1. **a:** The characteristic facial appearance. **b:** Long slender fingers. **c:** Generalized muscular hypotrophy with scapulae alatae.

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